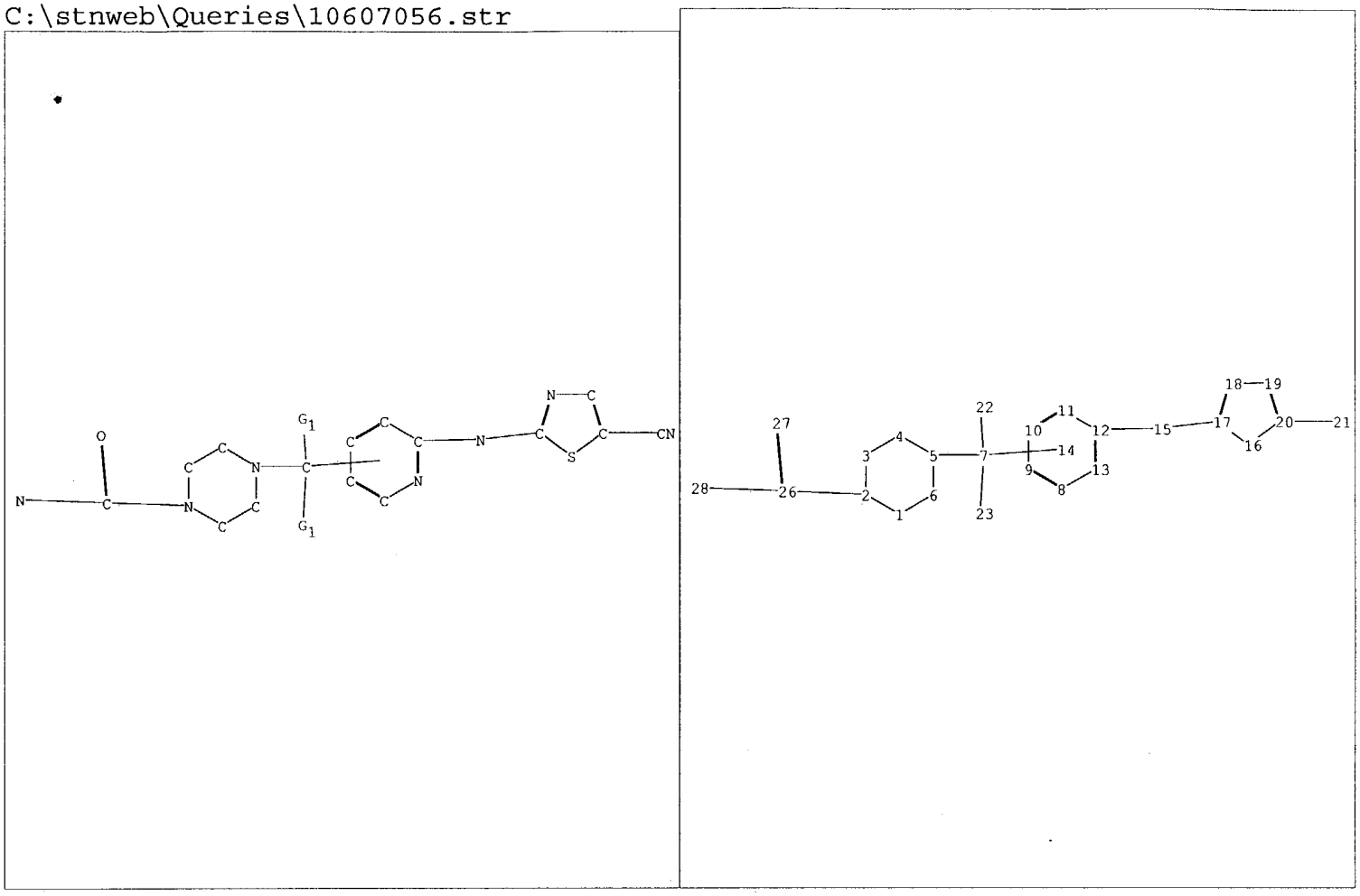
C:\stnweb\Queries\10607056.str



chain nodes :
7 15 21 22 23 26 27 28
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13 16 17 18 19 20
chain bonds :
2-26 5-7 7-22 7-23 12-15 15-17 20-21 26-27 26-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13 16-17
16-20 17-18 18-19 19-20
exact/norm bonds :
1-2 1-6 2-3 2-26 3-4 4-5 5-6 5-7 7-22 7-23 12-15 15-17 16-17
16-20 17-18 18-19 19-20 26-27 26-28
exact bonds :
20-21
normalized bonds :
8-9 8-13 9-10 10-11 11-12 12-13
isolated ring systems :
containing 1 : 8 :

G1:H,CH3

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:Atom 17:Atom
18:Atom 19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS 26:CLASS
27:CLASS 28:CLASS

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JUL 12   BEILSTEIN enhanced with new display and select options,
                   resulting in a closer connection to BABS
 NEWS  4  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS  5  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
 NEWS  6  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
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 NEWS  8  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS  9  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 10  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 11  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 27   STANDARDS will no longer be available on STN
 NEWS 13  SEP 27   SWETSCAN will no longer be available on STN
 NEWS 14  OCT 28   KOREAPAT now available on STN

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:16:12 ON 03 NOV 2004

=>
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter \"HELP COMMANDS\" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.31       2.31

FILE 'REGISTRY' ENTERED AT 18:22:38 ON 03 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
```

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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JUL 12   BEILSTEIN enhanced with new display and select options,
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 NEWS  4  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS  5  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
 NEWS  6  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
 NEWS  7  AUG 27   BIOCOMMERCE: Changes and enhancements to content coverage
 NEWS  8  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS  9  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 10  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 11  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 27   STANDARDS will no longer be available on STN
 NEWS 13  SEP 27   SWETSCAN will no longer be available on STN
 NEWS 14  OCT 28   KOREAPAT now available on STN

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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  of commercial gateways or other similar uses is prohibited and may
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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:16:12 ON 03 NOV 2004

=>
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter \"HELP COMMANDS\" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.31       2.31

FILE 'REGISTRY' ENTERED AT 18:22:38 ON 03 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
```

```
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     1 NOV 2004  HIGHEST RN 773835-43-1
DICTIONARY FILE UPDATES:    1 NOV 2004  HIGHEST RN 773835-43-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> index REGISTRY

AT LEAST TWO FILES ARE NEEDED FOR STNINDEX
SESSION CONTINUES IN THE PREVIOUS FILE ENVIRONMENT
To see a list of files and clusters that may be used in the INDEX
command, enter HELP FILE NAMES or HELP CLUSTER NAMES at an arrow
prompt.  Only the learning files and NBSFLUIDS may not be used in
STNINDEX.

=>
L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 18:23:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      4 TO ITERATE

100.0% PROCESSED       4 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            4 TO      200
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 18:23:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     97 TO ITERATE

100.0% PROCESSED      97 ITERATIONS                             20 ANSWERS
SEARCH TIME: 00.00.01

L3           20 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              155.42     157.73

FILE 'CAPLUS' ENTERED AT 18:23:29 ON 03 NOV 2004
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FILE COVERS 1907 - 3 Nov 2004 VOL 141 ISS 19
FILE LAST UPDATED: 2 Nov 2004 (20041102/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 6 L3

=> s l3/p
L5 6 L3/P

=> d l5 1-6 bib abs hitstr

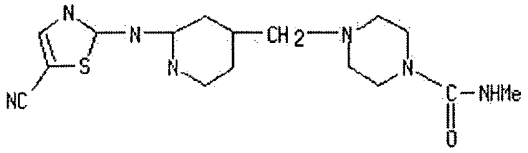
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2004:100813 CAPLUS
DN 140:151963
TI Salt forms with tyrosine kinase activity
IN Ren, Yu; Karki, Shyam B.; Zhao, Matthew M.; Bidodeau, Mark T.
PA USA
SO U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004023981	A1	20040205	US 2003-607114	20030626
PRAI	US 2002-398263P	P	20020724		

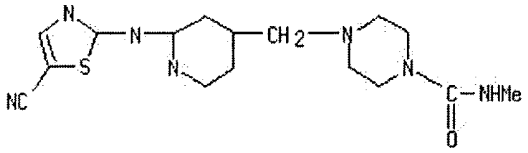
AB The present invention relates to salt forms of 4-[2-(5-cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide (I) which inhibit, regulate and/or modulate tyrosine kinase signal transduction, and compns. which contain these compds. Methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age-related macular degeneration, diabetic retinopathy, retinal ischemia, macular edema, and inflammatory diseases in mammals. Thus, I was prepd. by the reaction of a piperazine urea with formylpryridine-contg. aminothiazole deriv. followed by redn. The crystal structures of salts of I were studied.

IT **479611-82-0P 652156-19-9P 652156-20-2P**
652156-21-3P 652156-22-4P 652156-23-5P
652156-24-6P 652156-25-7P 652156-26-8P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(salt forms with tyrosine kinase activity)

RN 479611-82-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)

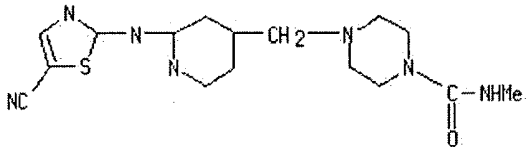


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 652156-19-9 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 652156-20-2 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monohydrochloride, monohydrate (9CI) (CA INDEX NAME)



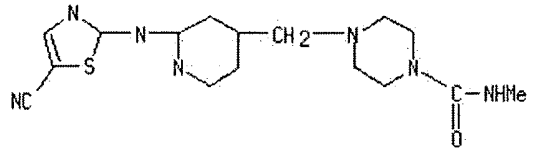
HCl

H_2O

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 652156-21-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monohydrochloride, compd. with ethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

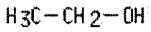
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

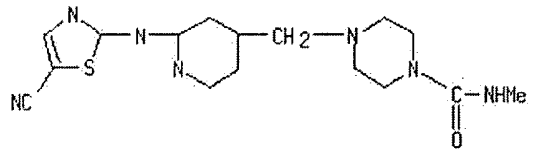
CRN 64-17-5
CMF C2 H6 O



RN 652156-22-4 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 479611-82-0
CMF C16 H19 N7 O S

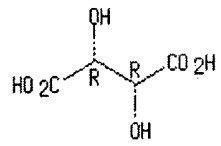


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

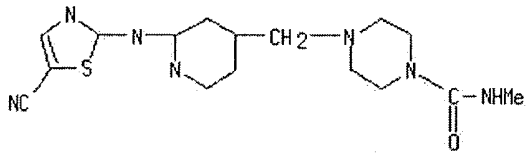


RN 652156-23-5 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 479611-82-0
CMF C16 H19 N7 O S

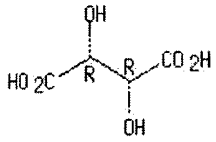


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 87-69-4
CMF C4 H6 O6

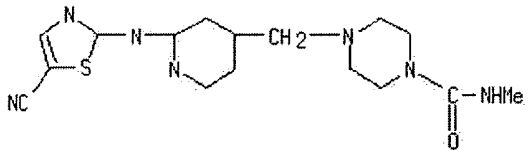
Absolute stereochemistry.



RN 652156-24-6 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

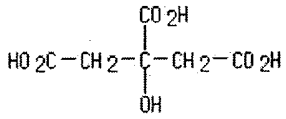
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

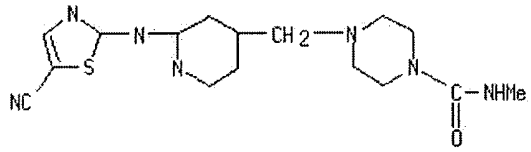
CRN 77-92-9
CMF C6 H8 O7



RN 652156-25-7 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1), monohydrate (9CI) (CA INDEX NAME)

CM 1

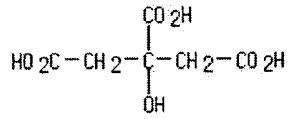
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

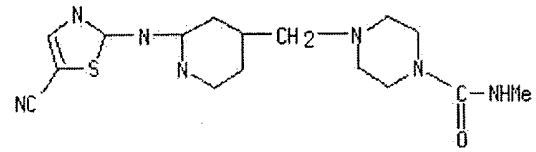
CRN 77-92-9
CMF C6 H8 O7



RN 652156-26-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monobenzenesulfonate (9CI) (CA INDEX NAME)

CM 1

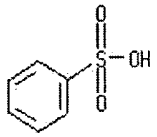
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 98-11-3
CMF C6 H6 O3 S



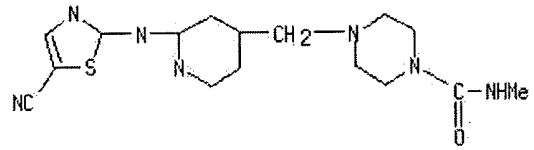
L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2004:100812 CAPLUS
DN 140:151962
TI Polymorphs with tyrosine kinase activity
IN Zhao, Matthew M.; Bilodeau, Mark T.
PA USA
SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004023980	A1	20040205	US 2003-607091	20030626
PRAI US 2002-398238P	P	20020724		

AB The present invention relates to active polymorphs of 4-[2-(5-cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide (I) which inhibit, regulate and/or modulate tyrosine kinase signal transduction, and compns. which contain these compds. Methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age-related macular degeneration, diabetic retinopathy, retinal ischemia, macular edema, and inflammatory diseases in mammal are also disclosed. Thus, I was prepd. by the reaction of BOC-piperazine with Me isocyanate followed by deprotection and reaction with 2-(4-chloromethylpyridin-2-ylamino)th-5-carbonitrile. The crystal structure of a I polymorph was studied.

IT **479611-82-0P**, 4-[2-(5-Cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-car boxylic acid methylamide
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorphs with tyrosine kinase activity)

RN 479611-82-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2004:100811 CAPLUS
DN 140:146127
TI Process for making substituted thiazolyl-amino pyridines
IN Zhao, Matthew M.; Yin, Jingjun
PA USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

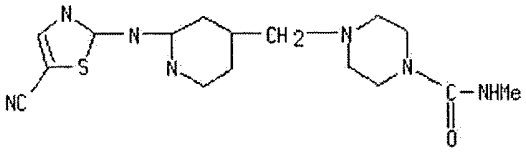
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004023979	A1	20040205	US 2003-607056	20030626
PRAI	US 2002-395837P	P	20020715		

OS CASREACT 140:146127; MARPAT 140:146127
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to a process for prepg. substituted thiazolyl-amino pyridines (I) [R = H, each (un)substituted C1-10 alkyl or aryl; R1 = CONHR3; R2 = H, OH, C1-6 alkoxy, C1-6 alkyl, halo; R3 = C1-6 alkyl] which are capable of inhibiting, modulating and/or regulating signal transduction of both receptor-type and non-receptor type tyrosine kinases and may be used to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, or inflammatory diseases in mammals. The above process comprises (a) prepg. a slurry of 2-aminothiazole-5-carbonitrile (II) (where R is defined above), 2-halopyridine-4-carbaldehyde (III) (where X = a halo; R2 is defined above) and a base in a solvent, (b) adding a palladium catalyst and a bisphosphine ligand to the slurry to produce a coupling product of 2-[(4-formyl-2-pyridyl)amino]thiazole-5-nitrile (IV), (c) adding a piperazine-urea of formula (V) (R3 is defined above) to the coupling product of formula IV; and (d) completing a reductive amination to produce the compd. of formula I. Thus, in a 2-3 kg scale reaction, 2-chloro-4-formylpyridine was coupled with 2-aminothiazole in the presence of Pd(dba)3, 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene, and K3PO4 in toluene-water at 90° for 8 h to give 97% 2-[(4-formyl-2-pyridyl)amino]thiazole-5-nitrile which underwent reductive coupling with N-(methylaminocarbonyl)piperazine hydrochloride using NaBH(OAc)2 in the presence of Et3N and AcOH in N,N-dimethylacetamide for a total of 260 min to give 80.4% the title compd. (VI). The compds. I inhibited VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values between 0.01-5.0 μM.

IT **479611-82-0P**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiazolylaminopyridines by amination of aminothiazolecarbonitrile deriv. with halopyridinecarbaldehyde deriv. to [(formylpyridyl)amino]thiazolenitrile deriv. and reductive coupling with N-(aminocarbonyl)piperazine deriv.)
RN 479611-82-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

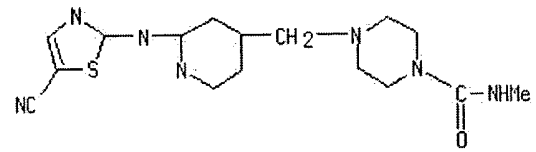
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2004:100810 CAPLUS
DN 140:151961
TI Active salt forms with tyrosine kinase activity
IN Ren, Yu; Karki, Shyam B.; Zhao, Matthew M.; Bilodeau, Mark T.
PA USA
SO U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004023978	A1	20040205	US 2003-607031	20030626
PRAI US 2002-398236P	P	20020724		

AB The present invention relates to orally active salt forms of the mesylate salt of 4-[2-(5-cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide (I) which inhibit, regulate and/or modulate tyrosine kinase signal transduction and compns. which contain these compds. Methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, retinal ischemia, macular edema, and inflammatory diseases in mammals are also disclosed. Thus, I was prepd. by the reaction of a piperazine urea with formylpyridine-contg. aminothiazole deriv. followed by redn. The crystal structures of salts of I were studied.

IT **479611-82-0P 652154-18-2P 652154-19-3P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(active salt forms with tyrosine kinase activity)

RN 479611-82-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)

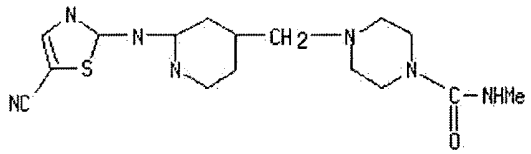


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 652154-18-2 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

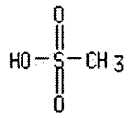
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

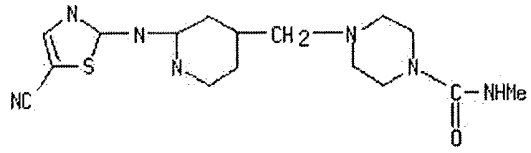
CRN 75-75-2
CMF C H4 O3 S



RN 652154-19-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl-, monomethanesulfonate, monohydrate (9CI) (CA INDEX NAME)

CM 1

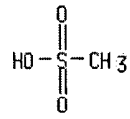
CRN 479611-82-0
CMF C16 H19 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

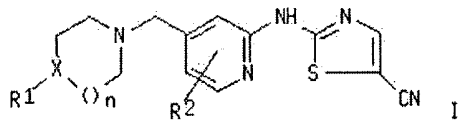
CRN 75-75-2
CMF C H4 O3 S



L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
Full Text
AN 2003:5956 CAPLUS
DN 138:73254
TI Preparation of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses
IN Bilodeau, Mark T.; Hartman, George D.
PA Merck Co., Inc., USA
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000687	A1	20030103	WO 2002-US21110	20020618
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1404672	A1	20040407	EP 2002-744810	20020618
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003100567	A1	20030529	US 2002-174774	20020619
PRAI	US 2001-300245P	P	20010622		
	WO 2002-US21110	W	20020618		

OS MARPAT 138:73254
GI



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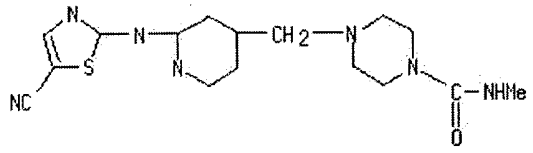
AB The present invention relates to thiazolylaminopyridines (shown as I; variables defined below; e.g. 4-[2-(5-cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide) which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals. For I: n is 0 or 1; X is C-H or N, provided X is C-H if n = 1 and R1 is SO2-(C1-C6 alkyl) and provided that X is C-H if R1 is NH(C:O)NR3H; R1 is SO2(C1-C6 alkyl), (C:O)NR3H, or NH(C:O)NR3H; R2 is H, OH, OC1-C6 alkyl, C1-C6 alkyl, or halo; and R3 is C1-C6 alkyl. Compds. I inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values = 0.01-5.0 μM. 4-[2-(5-Cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide, 2-[[4-[[4-(methylsulfonyl)piperidin-1-yl]methyl]pyridin-2-yl]amino]-1,3-thiazole-5-carbonitrile, and 4-[2-(5-cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide show enhanced

pharmacokinetic properties as compared to previously reported thiazolylaminopyridines in WO 01/17995 A1. Although the methods of prepn. are not claimed, 13 example prepns. are included.

IT **479611-82-0P**, 4-[[2-(5-Cyanothiazol-2-ylamino)pyridin-4-yl]methyl]piperazine-1-carboxylic acid methylamide **479612-56-1P**, 4-[2-(5-Cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide trifluoroacetate
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses)

RN 479611-82-0 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



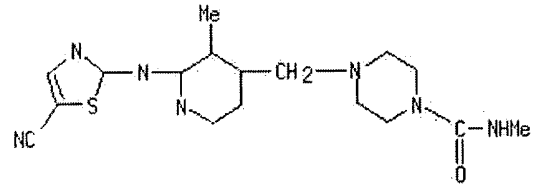
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 479612-56-1 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-3-methyl-4-pyridinyl]methyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

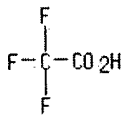
CRN 479612-55-0
CMF C17 H21 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

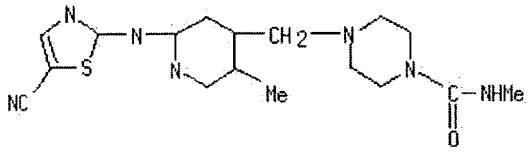
CRN 76-05-1
CMF C2 H F3 O2



IT **479612-28-7P**, 4-[2-(5-Cyanothiazol-2-ylamino)-5-methylpyridin-4-

ylmethyl]piperazine-1-carboxylic acid methylamide **479612-29-8P**, 4-[[2-(5-Cyanothiazol-2-ylamino)-5-methylpyridin-4-yl]methyl]piperazine-1-carboxylic acid methylamide trifluoroacetate **479612-55-0P**, 4-[2-(5-Cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide **479612-74-3P**, 4-[[2-Chloro-6-[(5-cyano-1,3-thiazol-2-yl)amino]pyridin-4-yl]methyl]-N-methylpiperazine-1-carboxamide **479612-92-5P**, 4-[[2-[(5-Cyano-1,3-thiazol-2-yl)amino]-6-ethylpyridin-4-yl]methyl]-N-methylpiperazine-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses)

RN 479612-28-7 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-5-methyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)

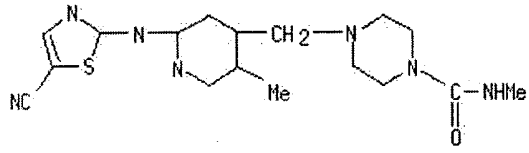


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 479612-29-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-5-methyl-4-pyridinyl]methyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

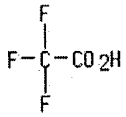
CRN 479612-28-7
CMF C17 H21 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

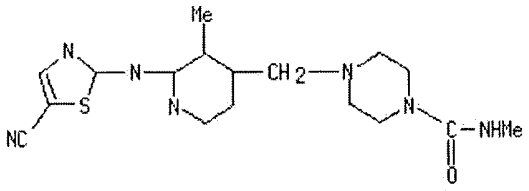
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 479612-55-0 CAPLUS

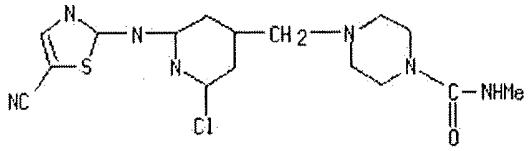
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-3-methyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 479612-74-3 CAPLUS

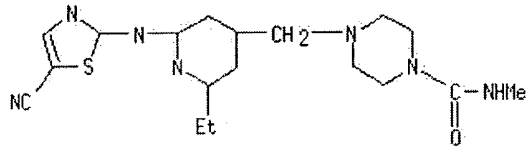
CN 1-Piperazinecarboxamide, 4-[[2-chloro-6-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 479612-92-5 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-6-ethyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

Full Text

AN 2001:185751 CAPLUS

DN 134:222709

TI Preparation of N-(pyrid-2-yl)-2-thiazolamines as tyrosine kinase inhibitors

IN Bilodeau, Mark T.; Hungate, Randall W.; Rodman, Leonard; Hartman, George D.; Manley, Peter J.

PA Merck Co., Inc., USA

SO PCT Int. Appl., 177 pp.
CODEN: PIXXD2

DT Patent

LA English

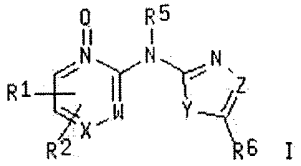
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2001017995	A1	20010315	WO 2000-US24432	20000906
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2000073517	A5	20010410	AU 2000-73517	20000906
	EP 1218376	A1	20020703	EP 2000-961583	20000906
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003509342	T2	20030311	JP 2001-522218	20000906
	BR 2000013899	A	20030708	BR 2000-13899	20000906
	EE 200200123	A	20030815	EE 2002-123	20000906
	US 2002147203	A1	20021010	US 2002-62351	20020201
	US 6586424	B2	20030701		
	US 2003064996	A1	20030403	US 2002-61817	20020201
	US 6586423	B2	20030701		
	BG 106465	A	20021229	BG 2002-106465	20020228
	ZA 2002001898	A	20030307	ZA 2002-1898	20020307
	NO 2002001166	A	20020425	NO 2002-1166	20020308
PRAI	US 1999-153348P	P	19990910		
	WO 2000-US24432	W	20000906		
	US 2000-658680	B1	20000908		

OS MARPAT 134:222709

GI



I

AB The title compds. [I; XW = CC, NC, CN; Y = O, S, NR4; Z = N, CR4; Q = O, absent; R1, R2 = H, OH, CN, etc.; R5 = H, SO2Rc, CO2Rc, etc.; R6 = aryl, CN, cycloalkyl, etc.; Rc = alkyl, cycloalkyl, aryl, heterocyclyl] which inhibit, regulate and/or modulate tyrosine kinase signal transduction, and therefore are useful in treating tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals, were prepd. Thus, refluxing 2-pyridylthiourea with (1-bromo-2,2-dimethoxyethyl)benzene in EtOH/HCl afforded the amine I [WX = CC; Y = S; Z = CH; Q = absent; R1, R2, R5 = H; R6 = Ph]. The compds. I inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 of 0.01-5.0 μM.

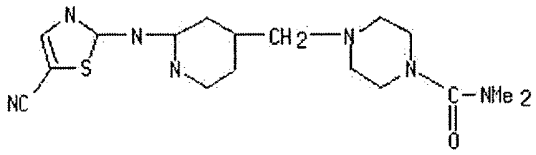
IT **329793-60-4P 329793-62-6P 329793-63-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(pyrid-2-yl)-2-thiazolamines as tyrosine kinase inhibitors)

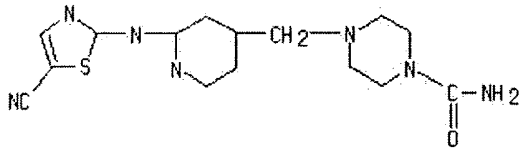
RN 329793-60-4 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-

pyridinyl]methyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



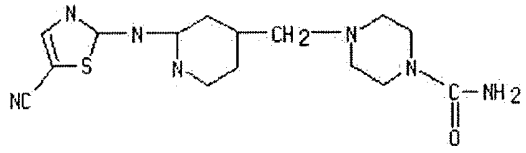
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 329793-62-6 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 329793-63-7 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

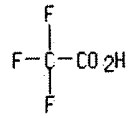
CRN 329793-62-6
CMF C15 H17 N7 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 76-05-1
CMF C2 H F3 O2



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